REMARKS

Claims 1-18 are pending in this application. Claims 1-18 have been subjected to a Restriction Requirement under 35 U.S.C. §121 and §372. The Examiner suggests that restriction of the present invention into the following groups is required.

Group I, claims 1-4, drawn to a pharmacophore model;

Group II, claims 5-11, drawn to a method for using a pharmacophore model to create an Na, K-ATPase inhibitory compound; and

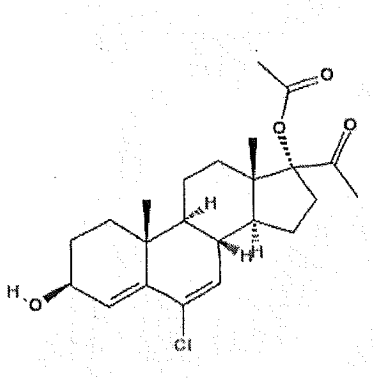
Group III, claims 12-18, drawn to a method of treating an individual with a heart disease.

The Examiner suggests that the inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical feature. Specifically, it is suggested that Group I is the technical feature that links Groups I-III; however, it is alleged that Group I is not a contribution over the prior art because it is suggested by references teaching a pharmacophore model of Na, K-ATPase, *e.g.*, Haller et al. cited in the International Search Report issued in the preceding PCT case. The Examiner asserts that lack of unity is present because the linking technical feature is not a special technical feature as defined by PCT Rule 13.2.

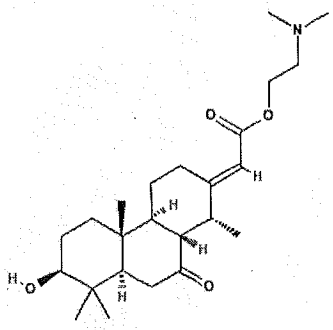
PCT Rule 13.2 indicates that where a group of inventions is claimed in one and the same international application, the requirement of unity of invention referred to in Rule 13.1 shall be fulfilled when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical

features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

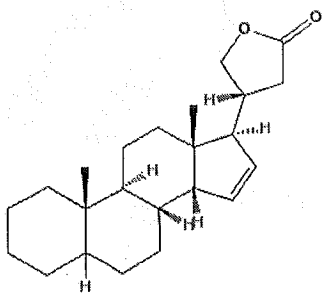
While the Examiner has cited Haller et al. as teaching a pharmacophore model of Na, K-ATPase, Applicants will assume, for the purposes of expediting prosecution, that the Examiner intended to refer to Holtje et al. ((1992) *Pharmazie* 47, abstract only) cited in the International Search Report mailed December 29, 2005. In contrast to the teachings of the present application, wherein a homology model of the extracellular loops and the transmembrane domains of Na, K-ATPases was created (See Figure 2) to generate a pharmacophore model for Na, K-ATPase inhibition (see Figure 4 and Tables 4 and 5), Holtje et al. disclose modeling the compounds themselves, without consideration of the features of the ligand binding pocket. Specifically, Holtje et al. suggest comparing digitalis-unlike compounds, such as chlormadinol acetate and cassaine, with cardenolides as a standard. The structure of these compounds, as obtained from the PUBCHEM Substance Database, is shown below.



Chlormadinol acetate



Cassaine



Cardenolide

As is clear from a comparison of the Holtje et al. compounds with compounds derived from the pharmacophore model of the present invention, *e.g.*, as in claim 3, the basic scaffold of the Holtje et al. compounds is distinct from those of the present invention. Thus, the pharmacophore model of the present invention, and compounds derived therefrom, cannot be held to be anticipated by the teachings of Holtje et al. Therefore, the pharmacophore model of the present invention is a special technical feature linking Groups I-III. As such, unity of invention exists and it is respectfully requested that this restriction requirement be reconsidered and withdrawn.

Were the Examiner to maintain this restriction requirement, it is respectfully requested that the restriction of Group I and Group II be reconsidered. In particular, it is respectfully submitted that a search of the pharmacophore model of Group I is coextensive with methods of using the same to create an Na, K-ATPase inhibitory compound. Indeed, any search pertaining to the claimed pharmacophore model will necessarily encompass all references which disclose how the pharmacophore model is used. Accordingly, the search and examination of more than one of the groups of claims would not be unduly burdensome. Accordingly, Applicants respectfully request reconsideration of this restriction requirement.

However, in an earnest effort to be completely responsive, Applicants hereby elect to prosecute Group I, claims 1-4, drawn to a pharmacophore model, with traverse.

Respectfully submitted,

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